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Disease-a-Month

Headache

JOHN R. GRAHAM

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Headache

JOHN R. GRAHAM

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John R. Graham

received his M.D. degree from Harvard Medical School and was an intern at the Massachusetts General Hospital. He took his residency training at the New York Hospital under Dr. Harold G. Wolff, with whose assistance he carried out experiments on the action of ergotamine tartrate in relieving the pain of migraine. From 1937, Dr. Graham worked as an assistant to Dr. George R. Minot for ten years in general medicine and was active in the Headache Clinic of the Massachusetts General Hospital. He has been Director of this Clinic since 1946. In 1950 he organized the Headache Research Foundation and during recent years has contributed several papers on migraine to the medical literature. He has lectured on the subject of headache to medical groups and in graduate courses at the Harvard Medical School. He is currently Chief of the Medical Service at Faulkner Hospital in Boston.

THE OBJECT of this treatise is to produce for the practicing physician a schema for the diagnosis, understanding and management of the patient who complains of headache. Since headache is a symptom of a myriad of medical disorders ranging through psychologic states, physiologic aberrations, structural abnormalities—or combinations of all three—it is necessary to impose limits to the scope of this discussion. The aim, therefore, will be to present enough information regarding present knowledge of the nature, mechanism and differential diagnosis of head pain to help the physician to place his patient in a proper category and to institute a rational form of therapy.

Although headache is one of man's most prevalent and ancient afflictions, knowledge of its various mechanisms has only recently emerged from the stages of magic, conjecture and empiricism and been increased by exposure to the experimental method. More fundamental understanding of headache has been gained in the past 25 years than in the previous 2,500 years. The information which is now beginning to come in is still far from complete and

undoubtedly will have to be revised many times in the future as the picture unfolds. The reader will need to keep this in mind as he scans the following pages, which should bear the railroad timetable warning, "Subject to Change without Notice." An elementary "headache timetable" has been evolved, however, and at least some of its trains of thought are running on a predictable and useful schedule.

GENERAL CONSIDERATIONS

Every organ in the body which is supplied with the receptors for pain becomes the site for the production of pain under the influence of certain pathologic states which are common enemies to many tissues. Such pathologic states include trauma, inflammation, ischemia, physical distortion and chemical alteration. In addition, many organs, by virtue of their specialized construction and function, are vulnerable to pain arising from influences peculiar to the individual organ. Thus, strong light may cause pain in the eye, hydrochloric acid pain in the peptic ulcer site, renal calculus pain in the ureter. Similarly, the head suffers pain, not only from the mechanisms which are common to all tissues, but also presents certain unique features which give rise to pains of a special nature.

In the first place, the head may become a source of discomfort in the neurotic patient just because it is the head—the "seat of reason," the home of the brain that traditionally is supposed to provide the answers to life's mental problems. Apparently, in some individuals, a failure to resolve conflicting emotional and mental problems is laid at the door of the responsible organ in the form of a variety of symptoms, such as "head fullness," "tightness," "pressure," "dizziness," "wooziness," inability to concentrate, and so on, all of which may be expressed by the patient as "headache."

The human head remains, for the most part, elevated above the rest of the body. This fact alone may account for many of man's headaches, inasmuch as it is probably responsible for a set of tissue pressure differentials, circulatory and metabolic controls in the brain and vascular anatomy which are different in the head from those in the rest of the body. Thus, when man is in

the erect position the venous pressure in his head is a minus figure, the circulation in his brain is chiefly controlled by CO_2, the autonomic control of cranial blood vessels is meager and the structure of intracranial vessels is less muscular than that of the more dependent portions of the vascular tree. Since it will become clear later in this discussion that the state of the cranial vascular tree has a great deal to do with certain types of headache, the consequences of man's head being above his heart take on significance in the matter of human headache. Teleologically speaking, the cranial circulation seems to have evolved in such a way as to insure that the brain in its point of vantage at the top of the body never lacks for an adequate blood supply. In this process the safeguards against an overdistention of the cranial vessels secondary to changes in systemic pressure or outside forces seem to have been less adequately provided than in other parts of the body. Thus the man who is swirled in the "human centrifuge" with his head away from the center develops a headache from the rush of blood into his cranial vessels but does not experience a "footache" when he is turned the other way about. Similarly, Marcussen and Wolff (1) in an ingenious series of observations have shown that the reactions of the cranial vasculature of circus performers who spend considerable periods daily standing on their heads are considerably different from those of more conventional mortals.

We must remember, also, that the head is a heavy globe balanced on a stack of movable, separate blocks—the cervical vertebrae. This whole loose assembly is held together by a system of muscles and ligaments which in themselves can become a source of head pain when overtaxed in their almost constant job of supporting the head and neck in all their complicated gyrations. Closely interwoven with these muscles and ligaments course the pain-sensitive vertebral and carotid arteries and the upper roots of the cervical and autonomic plexuses on their paths toward the cranium. Small wonder that their functions may be painfully disturbed by the strains and tensions that take place in this tightly packed cable—the neck! The head, balanced delicately on the neck, like an apple on a stick, by the inertia of its weight, becomes the source of painful trauma to its guy wires as the result of either a blow to itself, such as the headon football in-

jury, or a jar to the body below it, as in the all-too-common "whip-lash" injury. Because it is the seat of important organs of perception, such as the eyes and ears, prolonged periods of sustained and finally painful tension may be placed on its supports. Finally, when headache exists for any reason, immobilization of the head serves to keep pain at a minimum, and this very process of immobilization itself may become a subsidiary source of even more head and neck pain.

In a small, isolated community, the unruly behavior of an individual jostles the composure of the rest of the inhabitants more noticeably than in a large, expansive city. Within the "closed box" of the skull physical alterations in one compartment quickly affect the welfare of others. Thus, a localized increase in the size of a ventricle may quickly cause painful distortion of the tentorium; or, iatrogenic reduction of the spinal fluid volume may lead to painful compensatory expansion of the vascular compartment. A pea-sized cyst or tumor at a crucial spot may, for lack of room to expand in a harmless direction, impinge on exquisitely painful structures or block a vital channel, with resulting painful disruption of intracranial mechanics. Within the stable and sturdy structure of the skull is a 1,300 Gm. brain floating free in spinal fluid, like a mariner's compass within its box, except for its moorings, which keep it from swirling with every rotation of the head. These moorings consist chiefly of the great venous sinuses and their tributary veins, the large intracranial arteries, the falx and tentorium and the membranous envelopes of the meninges. All these structures are pain-sensitive and react with pain to mechanical stresses and, in the case of the vascular moorings, to alterations in their intrinsic physiology, or to both. As the brain floats in spinal fluid it weighs about 40 Gm. and it is with a tug of this degree that it pulls on its moorings when the head is jostled. If the spinal fluid is replaced with air, the brain suddenly is found to be tugging with its full weight of 1,300 Gm., and headache results.

Wolff and Ray (2) have made extensive observations on the pain sensitivity of the structures in the head. Their charts in the reference cited will supply the reader with detailed data should he desire it. Several salient points are worth noting here. In the

first place, the cranial vessels are a particularly important source of pain, whether they are inside or outside the skull. Although the pial arteries and veins are not pain-sensitive, all the vessels in the coverings of the skull and the great intracranial venous sinuses, their tributary veins, the meningeal vessels, the large intracranial arteries and their branches react with exquisite pain to traction, distention, direct pressure, trauma, inflammation, heat and electric stimulation. It is distortion and alteration of function of these vascular structures that are ultimately responsible for many of the head pains that result from space-occupying lesions, alterations in ventricular volume, intracranial hemorrhage and the headache of migraine, hypertension, fever, lumbar puncture and pneumoencephalography. The parenchyma of the brain itself, the lining of its ventricles, the choroid, the superficial pial vessels, and large areas of the meninges in themselves are not a source of pain, but produce headache chiefly by means of secondary disturbances in their relation to neighboring vascular structures. Wolff has pointed out that pain arising from sources within the skull is brought about chiefly by 6 mechanisms:

"(*1*) Traction on the veins that pass to the venous sinuses from the surface of the brain and displacement of the great venous sinuses; (*2*) traction on the middle meningeal arteries; (*3*) traction on the large arteries at the base of the brain and their main branches; (*4*) distention and dilatation of intracranial arteries; (*5*) inflammation in or about any of the pain-sensitive structures of the head; and (*6*) direct pressure by tumors or adjacent tissue on the cranial and cervical nerves containing many pain-afferent fibers from the head" (3).

To these might be added the as yet unknown disruption of physiology which causes the intrinsic neuralgias of the fifth, seventh and ninth cranial nerves.

Pain arising from structures inside the cranium "on or above the superior surface of the tentorium cerebelli results in pain in various regions in front of a line drawn vertically from the ears across the top of the head. The pathways of this pain are contained in the fifth cranial nerve. Stimulation of the pain-sensitive intracranial structures on or below the inferior surface of the tentorium cerebelli results in pain in various regions behind the

line just described. The pathways for this pain are contained chiefly in the ninth and tenth cranial and the upper three cervical nerves" (4).

Occasional exceptions to this statement may be found in the case of unusual forms of facial and otic pain which may use the pathway of the sensory division (nervus intermedius) of the seventh cranial nerve. It may ultimately be shown, also, that some sensory nerves in the head find their way to the central nervous system by routes other than the fifth, sixth, ninth and tenth cranial nerves and the upper three routes of the cervical plexus. Certain baffling problems in head pain exist even after the fifth, seventh and ninth and upper three cervical nerves are cut. For the most part, sensory fibers travel in the head either in nerve bundles or along vascular channels until they reach a suitable main sensory trunk, at which point they leave the vessels and join the nerve. Possibly some sensory fibers may continue along vessels and find their way into the cord, low in the neck. Autonomic fibers which ride the "vascular rails" are motor rather than sensory and their surgical extirpation leads to alteration in function rather than perception of the affected part.

It is of special interest that pain arising from stimulation of many intracranial and extracranial structures may be referred to the region of the homolateral eye, and may lead the patient to the ophthalmologist. (These structures include the superior sagittal sinus, its tributary veins, the anterior and middle meningeal arteries, the temporal and supraorbital arteries, the anterior, middle and posterior cerebral arteries, the internal carotid artery and sylvian vein.)

Similarly, the otolaryngologist may be sought by the patient who really has disturbances in the vicinity of the pontine, internal auditory, posterior inferior cerebellar, vertebral arteries and the undersurface of the tentorium, since the reference of pain arising in these structures is to the region of the homolateral ear and just behind it. The otolaryngologist may also be called in for the treatment of a "sinus headache" which is in reality a headache of the migrainous order associated with dilatation of the internal maxillary artery, vascular congestion of the sinus and nasal membranes and secondary blocking of the nasal airways. Hunter and Mayfield (5) have shown that irritation of the sec-

ond and third cervical sensory roots can cause pain, not only in the occiput and neck, but also in the region of the eye and temple. Thus, it is clear that structures within the cranial cavity and in the neck can produce pain simulating local ophthalmic, nasal and otic disorders.

Conversely, localized disease in the eye may secondarily result in painful muscle spasm in the temple, forehead and neck; disturbances in the region of the ostia of the accessory sinuses (which are by far the most pain-sensitive areas in the nasal airways) may be registered in the eye, temple and vertex, and even a diseased tooth may cause pain which is referred to the temple or forehead. When, however, local disorders of the eyes, teeth, nose and ears cause referred pain in remote areas, it is rare in my experience that pain is not also felt in the immediate vicinity of the diseased organ itself. Thus, for instance, one should hesitate to attribute a pain in the left temple to a third molar which is shown by x-ray to be impacted unless there are local symptoms and signs in the immediate neighborhood of the tooth. The same may be said in most instances for "retained root fragments," antral cysts, swollen turbinates, diseased sinuses and ophthalmic disorders. Various teachings from the past have indicated that disturbances of bowel, gallbladder and uterine function cause "referred" pain in the head. Except insofar as disorders of this type may give rise to psychologic states, vasomotor reactions, endocrine abnormalities and febrile or toxic reactions which may secondarily produce headache, these remote organs do not cause "referred" pain in the head and should not be removed in an effort to cure headache.

DIAGNOSIS, MECHANISM AND TREATMENT OF VARIOUS TYPES OF HEADACHE

The classification of headaches which proves most useful to the practicing physician is one which depends heavily on the pathology or pathologic physiology of the various forms of headache (insofar as they are known), and also takes into account important features of their clinical manifestations and natural history. Systems of classification which in the past have depended entirely on clinical features of the syndrome have not provided sufficient

understanding of physiologic mechanisms to form a basis for rational therapy. On the other hand, the physician in his office faced by a patient with a headache must depend to a large extent on the history and physical findings in order to begin the process of identification of the disease at hand which will lead to fruitful investigation and treatment of its pathologic mechanism. Some syndromes which are clinically similar in the nature, location and duration of the pain may be due to entirely dissimilar mechanisms—and, conversely, others which have mechanisms which are closely related may present natural histories or clinical pictures which are so unlike that they deserve a separate identity. Thus, the headache of the migraine attack and that of the leaking aneurysm may be so similar as to lead to confusion of one with the other, although the pathologic processes involved are different. On the other hand, the disturbed vascular physiology of atypical facial neuralgia, Horton's syndrome, and migraine may be closely related, but the clinical behavior of these disturbances in the patient is so different that each one deserves a place of its own in a practical classification of headache. For these reasons, the classification given below takes into account both clinical and pathologic features. A reminder should be made that our knowledge of headache mechanism is far from complete. Because this is so, we should not be too quick to ascribe headaches of unknown etiology to psychogenic causes unless there are positive indicators pointing toward anxiety and tension as important influences.

It seems worth while to dwell briefly on some of the features of the patient's description of his headache which are useful to the physician in evaluating the nature of the problem at hand. In the first place, the degree or severity of the pain is important. Although the human threshold to pain is remarkably constant, the total human reaction to a given painful stimulus varies greatly from person to person. An evaluation of the severity of pain may be approached by a consideration of how it interferes with the patient's activity: whether it makes him go to bed and give up work; whether it can be controlled by aspirin, empirin® and the ordinary analgesics; whether it leads to nausea, vomiting, diarrhea and general prostration. For instance, a migraine attack is prone to resist ordinary analgesics and to cause disabling side effects, whereas a tension headache can usually be quelled with

empirin® or aspirin and is compatible with continued activity.

Determination of the type of pain is of use in diagnosis. Some "headache," on close examination, turns out not to be an "ache" at all, but rather a "fullness," "tightness," "band on the head," "pressure" or "drawing" sensation, characteristic of the tension state. Other headaches may present a pulsating or throbbing quality which indicates a vascular component. The lancinating, "electric shock" jab of pain is not only characteristic of the true neuralgia or "tic" type of headache, but is a prerequisite for this diagnosis. Soreness and a steady, drawing ache in the neck muscles are characteristic of the spasm of cervical and scalp muscles which occurs in the "tension" headache.

The manner of onset and offset and duration of the headache may be a lead to its diagnosis. Thus, the ache of migraine is usually gradual and slow in its build-up and disappearance and usually lasts a matter of several hours or days compared with the sudden precipitous, overwhelming onset of tic and its equally sudden cessation, or the hammerlike blow of the subarachnoid hemorrhage, or the rapid, 5-to-10-minute development of the "Horton's" attack and its tendency to endure through a range of a few minutes, or at most 1, 2 or 3 hours with recurrences, several times, perhaps, in the same day or night. The headache or head discomfort of the tension state or conversion hysteria characteristically may go on interminably for days, weeks, months and years without a free moment as opposed to the headache of brain tumor which in only rare instances fails to leave the patient with periods of respite.

A history of the timing and precipitants of head pain is a powerful aid in determining its cause. Thus, the tendency for migraine to follow as an aftermath of fatigue and strain, changes of pace in living, emotional disturbances and sleep is in contrast to the behavior of the headache of organic intracranial disease which pays little respect in its inevitable progress to such changes in the life situation of the patient. The history of the behavior of the headache throughout the life of the patient may be helpful. A story of headache beginning for the first time in a man of 50 points much more in the direction of organic intracranial disease, arthritis of the cervical spine or an inflammatory process than the life-long migrainous process firmly entrenched with

roots in a positive family history, the successive development of carsickness, cyclic vomiting attacks in youth, and the periodic occurrence of "sick" headaches against a background of otherwise good health over the adult years, or the "batch" or "cluster-

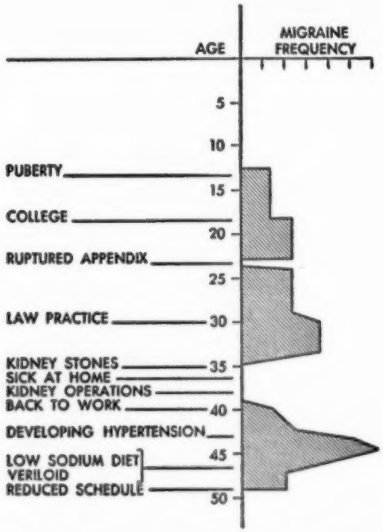

FIG. 1.—Migraine frequency plotted against life situations. Increase of stress in college and during law practice led to more frequent attacks, whereas illness of varying sorts led to freedom from migraine.

(Figures 1 to 4 reproduced from J. R. Graham, *Treatment of Migraine*, by permission of Little, Brown & Company, Boston.)

like" character of the attacks of "Horton's" headache in which months or years of freedom are punctuated by weeks of daily recurrent attacks. Relief of headache during pregnancy, operations and intercurrent illnesses will characterize the migraine victim, whereas under similar conditions the tension state may be made worse and organic disease aggravated or brought into the open for the first time. The beneficial effects of travel or

vacation may reveal the non-organic nature of the headache syndrome and, conversely, failure to find decrease of headache under improved conditions of living may arouse suspicions of organic disease as a cause for headache. The total effect of the headache experience on the patient may contribute to discovering its cause. Thus, the migraine attack characteristically makes the patient withdraw from people, confusion, light and noise and seek the seclusion of a dark, quiet room, whereas the "Horton's" headache or tic may drive the patient to frantic pacing of the floor or crying out loud in lonely nocturnal vigils, and the pain of the brain tumor or ruptured aneurysm cause the patient to seek frantically for medical help because the nature of this new experience instinctively makes him feel that something is "vitally wrong" with him.

The symptoms and signs which accompany head pain may be of vital importance in its differentiation. The nausea, vomiting, polyuria, diarrhea and prostration of the migraine attack present a totally different picture from the nagging insistence but relative lack of incapacitation of the tension state. Evidence of stiff neck, fever, and serious neurologic derangement point toward organic intracranial involvement and signs of inflammation in an eye, tooth or sinus may be the indicator of localized disease as a cause. Observation of a patient during an attack of headache may reveal etiologic mechanisms through the appearance of dilated extracranial arteries or relief from manual compression of temporal, occipital or carotid vessels (as in migraine), or the facial flushing, Horner's syndrome, tearing of the eye and a blocked nose in the "Horton's" headache, or the tense, knotted, painful cervical muscles relieved by head traction in the tension state, or the stiff neck and fever of meningitis and subarachnoid hemorrhage. The effect of drugs in relieving headache by means of their vasoconstrictive, vasodilating, muscle-relaxing or analgesic qualities, and the effect of local anesthesia with procaine may also provide insight into the fundamental nature of the disease process.

Bearing these facts in mind, let us proceed to a consideration of the different categories of headache, their diagnosis, mechanism and treatment.

LOCAL CAUSES OF HEADACHE

The Eyes

It is traditional for the headache victim to attribute headache to eye difficulties and to seek help first from the ophthalmologist. Experience reveals, however, that the patient who presents a "headache problem" only occasionally finds relief from this source. When refractive errors cause head pain, the discomfort is usually clearly related to intensive use of the eyes and occurs in their immediate vicinity. Prolonged strain of the intrinsic muscles of the eyes in patients who suffer from muscle imbalance or hypermetropia may lead to pain in the eyeball and spasm of the muscles of the scalp in their immediate vicinity, and, in some cases, of pain-sensitive cervical muscles. These symptoms are usually related immediately in time to the use of the eyes. Myopia rarely causes headache and slight refractive errors of other types are infrequently a cause. Intrinsic diseases of the eye, such as glaucoma, ulceration of the cornea and iritis may be a source of severe eye and head pain, but are usually accompanied by local signs of irritation in the eye, which point to that organ as the seat of the trouble. Correction of refractive difficulties in patients with migraine and tension headaches is important in relieving the patient's total burden of fatigue, but is only one step in total therapy. The headache which follows the viewing of a movie has many of its roots in the emotional components of the experience as well as the ocular strain. The fact that headache is accompanied by photophobia does not indicate necessarily a refractive error as a cause for headache, since this symptom along with an aversion to loud noise, confusion and strong odors is more commonly a manifestation of the heightened irritability of the nervous system which accompanies many types of head pain. Thus, the eyes should always be considered in the treatment of headache, and refractive errors or local pathologic conditions corrected; but repeated changes of lenses and multiple visits to the ophthalmologist should be discouraged once a good opinion has been obtained and proper therapy instituted.

The Nose, Sinuses and Ears

When the diagnosis of headache due to disorders of the intranasal structures is made, evidence of localized disease in the nose

should be present. The membranes covering the turbinates and in the vicinity of the ostia may be the source of severe head pain when they are inflamed by bacterial or viral infections, or when they are impinged on by direct pressure or distorted by pressure differentials between two nasal chambers. Incrimination of infection of the intranasal cavities as a cause of headache should be corroborated by the presence of clinical evidence of infection, such as reddened, swollen membranes, purulent discharge, fever or regional tissue-swelling and tenderness and x-ray findings of a pus-filled antrum or regional osteomyelitis. Many headaches of vascular or migrainous origin masquerade for years as "sinus" headaches because the vascular dilatation which is the main feature of their mechanism is accompanied, in the nose, by a swelling and engorgement of nasal mucous membranes which leads erroneously to considering them as the cause rather than "a part" of the headache. When corroborative signs of infection are present, proper antibiotic therapy and measures to promote drainage are in order. When they are not, decongestive measures, puncturing of antral walls, sinus operations and removal of turbinates not only do no good, but may, in fact, lead to sinus disease which had not been present before. That engorgement of nasal membranes per se, by processes other than inflammation, is rarely the cause of headache is well demonstrated by the infrequency of headache in patients whose noses are thoroughly blocked by hay fever and vasomotor rhinitis.

The airplane passenger, by virtue of his rapid transit from one barometric pressure to another, especially if his nasal membranes are swollen and inflamed by infection or allergy, may create pressure differentials between his nasal cavity and its accessory sinuses and middle ear, and thus create headache by distortion of the sensitive membranes which surround the openings of these cavities. Apparently such headaches may rarely occur, without barometric changes, through blockage of an ostium by swollen membranes and absorption of oxygen by the blood stream from the trapped sinus. Headaches of this variety which have been called "vacuum headaches" are quickly relieved by nasal decongestion with neo-synephrine® sprays and insufflation of the Eustachian tubes.

Nasal polyps and antral cysts are infrequently the source of headache and, consequently, operations on these structures should

be based on otolaryngologic indications, rather than anticipation that recurrent headache will thereby be relieved. Neoplasms of the nasal cavities and pharynx may be the source of extremely severe headache once they begin to invade pain-sensitive tissues. That the sensory pathways of the head are devious and complicated is occasionally illustrated by certain instances of advanced nasopharyngeal cancer in which head pain persists even after section of the fifth, seventh, ninth and tenth cranial nerves and upper three cervical roots.

Headache arising from local disease in the ear is usually accompanied by visible signs of inflammation in the outer or inner ear, swelling or retraction and redness of the drum, interference with hearing and evidence of inflammation elsewhere in the nasopharynx. Chronic inflammation in the ear, petrous tips and mastoid rarely causes headache and should be well documented by history, physical findings and x-ray evidence before being approached surgically for the relief of pain. The reader is reminded of the numerous intracranial structures in the region of the internal auditory artery, the lower surface of the tentorium and the basilar and vertebral system of arteries and cervical plexus, all of which refer pain to the region of the ear and just behind it when stimulated by disease processes and which should be seriously considered when ear pain is confronted in the absence of obvious local disease of the ear.

The Teeth and Jaws

Wolff (6) has shown that stimulation of a tooth with electric current causes pain not only in the tooth itself, but headache in the face and temple on the affected side, often lasting for a considerable time after the noxious stimulation and local pain have ceased. This experimental evidence and certain clinical experiences indicate that at times headache due to dental disease may be experienced in areas remote from the local source. Recurrent headaches of this sort from impacted third molars have been reported especially in the age group from 17 to 25, when the molars are pushing through (7). Many more examples, however, of teeth being extracted as a supposed cause of remote headache without benefit might be quoted. It is not at all uncommon to

find that pain in a tooth is a part of the migraine or vascular headache attack. By and large, headache of dental origin is usually accompanied by pain or sensitivity in the tooth itself which will lead to proper dental attention. The removal of teeth for relief of headache remote from a supposed dental source and not accompanied by local symptoms in the tooth should be approached with a conservative attitude, after thorough investigation of all other possibilities.

Headache resulting from malocclusion and disorders of the temporomandibular joint has been reported by Costen (8), usually in elderly patients who lack back teeth and have a severe degree of overbite which strains the pain-sensitive structures in the vicinity of the jaw joint. Such patients may have not only headache, but neuralgia and paresthesias within the mouth and disturbances of hearing. Although this syndrome is rare, it should be remembered in patients who present marked degrees of malocclusion.

Disorders of the Neck

Every patient who presents a headache problem deserves thorough consideration of disorders of the neck as either a primary source or contributing agent in the production of head pain. Structures in the neck such as the upper three cervical posterior nerve roots and the carotid and vertebral artery systems not only provide the pathways over which pain from disease in the head may be registered, but also in themselves, under the influence of noxious stimuli, may produce head pain. The cervical muscles may develop painful spasm and secondary painful ischemia in response to headache arising from intracranial and extracranial sources and thus contribute to the headache of eyestrain, sinus disease, migraine and intracranial tumors, or they themselves may initiate head pain through spasm resulting from tension states or disease processes within the neck. Thus, the neck is on both the receiving and sending end of head pain. Examination of the neck as a source of headache should include observation of the size, sensitivity to pain and even the sound of the carotid arteries. Muscle spasm, points of muscle tenderness, neck posture and limitation of motion should be checked. Scoliosis of the

upper thoracic spine may throw the rib cage higher on one side than the other, causing painful pressure on the brachial plexus and reflex spasm in neck muscles. Palpation of the supraclavicular area may reveal tumors, tight scaleni and cervical ribs which may instigate head pain. Traction on the head during a headache may reveal an important contributing element of cervical spasm. An x-ray search is worth while for marked cervical arthritis, spurs impinging on the neural foramina as revealed in oblique views, straightening or reversal of the normal cervical lordosis, pathologic narrowing of interspaces and the presence of cervical ribs, or destructive processes in the architecture of a cervical vertebra from intrinsic or metastatic tumor. Such findings must be correlated closely with the clinical history and description of the headache, since many patients prove to have marked arthritic and intervertebral changes as age advances and yet have no neck or head pain. When headache is a problem, however, and other explanations are unsatisfactory and the history is consistent with a neck lesion, attention to this area may be rewarding. Surgical extirpation of cervical ribs, impinging spurs and ruptured intervertebral disks is indicated only if they can be related clinically to the head pain. A conservative preliminary approach by means of heat, physiotherapy, massage, exercises and head traction is recommended. Much has been written concerning the relief of a migraine-like syndrome involving unilateral head pain by means of either repeated injections of novocain® in the occipital and upper cervical regions (9), or by repeated head traction (10). Such measures may be worth a trial, but prolonged success has been lacking in our hands, if the process is really due to a vascular cause as in migraine, rather than to a definite physical abnormality in the neck. Operations for the relief of "occipital" neuralgia should be preceded by repeated demonstrations of relief of the pain by procaine block. Even when this has been convincingly shown, certain patients fail to get relief following operation, and subsequently bother their physician with complaints about postoperative paresthesias in the area involved.

CRANIAL INFLAMMATION

The headache which accompanies meningitis due to a number of different agents (viruses, bacteria, treponema, fungi) arises

from direct stimulation of the sensitive areas of the meninges at the base of the brain, direct involvement of sensitive cranial arteries and, at times, by distortion of pain-sensitive structures from localized alterations of cerebrospinal dynamics. It is usually accompanied by fever and signs of toxicity, neurologic involvement and stiff neck. It is the stiffness of the neck which is most frequently left unexamined. Treatment of the headache is fundamentally that which is indicated for the underlying disease. Use of powerful respiratory depressants should be avoided and, if possible, codeine, the salicylates, caffeine and mild sedatives employed for the relief of pain. At times, temporary relief may be gained by the judicious use of lumbar puncture drainage.

Cranial arteritis, as described originally by Horton *et al.* (11), deserves special consideration in this category, because when it exists it is frequently missed and, conversely, the diagnosis is sometimes made erroneously in prolonged headache states. Usually it occurs in middle or later life and is characterized not only by persistent headache, but also by signs of generalized toxicity, such as fever, elevated white count and sedimentation rate, and by the presence of swollen, tender, pulseless arteries and, at times, by neurologic complications, including mental confusion and visual and auditory disturbance. The development of prolonged daily headache in an elderly person who has not suffered from headache in the past, the presence of generalized malaise and fever and the discovery of nodular, swollen, painful arteries in the temporal or occipital regions are features which point to this diagnosis. Surgical removal of the involved artery often provides not only the diagnosis but also relief. In some cases the use of salicylates in ample quantities is sufficient to control the disease until it has run its course, but in cases in which neurologic complications are threatening, cortisone or ACTH may be used to advantage. It is conceivable that anticoagulants such as heparin and dicumarol® may also have a place in severe cases since significant damage usually arises from thrombosis of involved vessels.

SPACE-OCCUPYING LESIONS

Brain tumors, abscesses, cysts, hematomas and other space-occupying lesions within the skull cause headache chiefly by distortion of pain-sensitive structures in their immediate vicinity

(usually arteries, venous sinuses and their tributary veins), by direct pressure on sensory nerves or pain-sensitive vascular channels or by the effect of local cerebrospinal fluid pressure changes in distorting pain-sensitive structures remote from the lesion. In the stage of development of the lesion before significant alterations in cerebrospinal dynamics have taken place, the location of the head pain is a fairly reliable indicator as to the position of the lesion. Thus, headache on the left probably indicates tumor on the left, headache in the front of the head means tumor above the tentorium and headache in the occiput means tumor below the tentorium. When secondary pressure alterations develop, however, and there are signs of increased intracranial pressure, the "diagnostic localizing" value of the location of the headache rapidly diminishes, since remote effects which can be misleading come into play. Since posterior fossa lesions cause such alterations earlier than supratentorial tumor masses, the diagnostic value of the headache's location in such lesions is likely to be short-lived.

When headache occurs as a symptom of a space-consuming lesion, it is usually associated with other symptoms of serious neurologic disturbance which serve to point toward organic intracranial disease as its cause. In about one third of the cases, however, headache may be the only symptom of such a lesion for a protracted period before the symptoms of disordered brain function appear. At this stage, the physician is taxed indeed to discriminate this type of headache from more "functional" varieties. The failure of brain tumor headache to follow the course of the natural history and clinical behavior of the functional disorders may be the main clue to correct and early diagnosis. Thus, the brain tumor headache may develop suddenly and increase insistently in severity and frequency out of a "headache-free" sky, whereas the migraine victim usually provides a family and personal history of headache episodes or migraine equivalents which stretch periodically back over his medical history. The disregard of the tumor headache for time, place, emotional strain and other ordinary precipitants of tension and vascular headache may be significant. The insistence of the puzzled patient that something that he has never experienced before is wrong with him and the testimony of his relatives that such headaches are totally out of keeping with his character and life situation may be

subtle but useful diagnostic straws. Sudden and repeated episodes of headache in a child or in an adult for the first time, constant recurrence of the pain in exactly the same site and a rapid march in the severity of the attacks should make one consider seriously the possibility of organic disease.

The development of neurologic symptoms and signs in association with headache should arouse suspicion regarding an organic etiology. To be sure, the classic migraine attack is ushered in by dramatic symptoms of this sort, such as half vision, aphasia, hemianesthesia, and so on, but these usually clear as the headache comes on. In migraine, with a few exceptions, these symptoms are usually disturbances in sensory perception. Motor involvement such as ophthalmoplegia and unilateral paresis are rare and should be viewed with suspicion.

When neurologic dysfunction appears in the midst of headache rather than as a premonitory warning, and certainly when it persists for hours or days after the headache, thorough investigation for an organic cause is indicated. Epileptic seizures or periods of unconsciousness occurring in association with headache demand similar exploration. Skull x-rays and brain wave tests may be conducted in such patients on an out-patient basis, but more serious procedures, such as lumbar puncture and pneumoencephalography should be performed only within a hospital after careful consideration of the possible dangers attendant on disturbing intracranial pressure and volume relations.

Treatment of intracranial space-occupying lesions cannot be discussed here and is left to the realm of the neurosurgeon.

ORGANIC INTRACRANIAL VASCULAR LESIONS

Hemangiomas, arteriovenous fistulas and aneurysms may produce headache of either an intermittent or, less often, a steady type. Mechanisms of such pain include distortion of neighboring pain-sensitive structures and direct pressure on sensory nerves, but more commonly consist of intravascular dilatation and painful stretching of the walls of the lesion itself or episodes of hemorrhage. A bruit heard over the head, carotid vessels or eyeball, pulsation of an eyeball, recurrence of pain in exactly the same site and development of stiff neck or signs of neurologic impair-

ment during or following a headache make such a diagnosis likely. Some of these patients, unfortunately, have a history of migraine too and, in fact, there is some reason to feel that the attacks of pain which arise from stretching the vascular coats of these abnormal vessels may be emphasized or actually precipitated by the cranial vascular dilatation that occurs in the painful phase of migraine. A sudden, dramatic change in the severity of migraine or the occurrence of stiff neck, prolonged mental confusion, coma and fever and the development of abnormal reflex changes during a supposed migrainous attack may be the leads to the diagnosis of a subarachnoid hemorrhage from a serious vascular abnormality of this sort. Here, again, lumbar puncture, if performed for diagnostic purposes, should be made with caution and in a hospital. Management of such lesions lies in the realm of the neurologist and neurosurgeon.

CEREBROVASCULAR ACCIDENTS

Disturbances of neurologic function rather than headache are likely to comprise the prominent clinical features of cerebral vascular accidents such as embolization, thrombosis and hemorrhage. Many episodes of cerebral thrombosis are unaccompanied by pain and even when pain is present it is rarely severe. The mechanism of the pain in both thrombosis and embolization is probably twofold—distention and ischemia of the walls of the involved vessel and compensatory dilatation of neighboring arteries. The latter mechanism has been suggested by Denny-Brown (12) as the cause of headache in those patients who have suffered both gradual and abrupt narrowing of the carotid and basilar artery systems. The pain associated with cerebral hemorrhage is more likely to be severe (while the patient is conscious) and is caused not only by distention and ischemia of the involved vessel, but by the distortion of neighboring sensitive structures by the growing mass of the hemorrhage. It is well to remember that hypertension in discovered cases of cerebral hemorrhage may be the result as well as the cause of the hemorrhage. Certain patients in this group may not pursue the usual rapidly fatal course, but may level off to an equilibrium during which skull x-rays can be obtained which may show displacement of a calcified pineal.

This may suggest the presence of a localized intracerebral clot which in expert neurosurgical hands may be successfully evacuated.

POST-TRAUMATIC HEADACHE

Headache is a prominent symptom of the syndromes which follow head injury. Four general subdivisions of this subject may be made, each of which may be complicated by overlapping factors from all or any of the others.

1. *Headache Secondary to Epidural or Subdural Hemorrhage* (13). Head pain resulting from epidural hemorrhage is due to distortion of and pressure on the pain-sensitive meningeal vessels which have been ruptured by the injury and their neighboring venous sinuses. The development of headache goes hand in hand with the rapid and steadily progressive development of neurologic signs and symptoms which take place as the hemorrhage dissects and distends the space between the skull and the dura and presses on the brain. X-ray evidence of a fracture across the site of meningeal vessels plus the rapid, steady progression of neurologic signs and increasing headache until coma supervenes suggest this source for the headache. In the case of subdural hematoma, on the other hand, the classical history of unconsciousness due to concussion, followed by a lucid period of hours, days or weeks and the subsequent relapse into coma or development of chronic headache and evidence of neurologic degeneration is more often the rule. The sequence of events in this situation is of great diagnostic importance and conforms to the expected consequences of slow bleeding from lacerated tributary veins and venous sinuses, the formation of an osmotically self-increasing hygroma and its gradual distortion of pain-sensitive structures and impingement on important neurologic structures. Unfortunately, the telltale history of a significant head injury is not infrequently lacking in cases of chronic subdural hematoma, and the diagnosis has to be based on a history of headache and neurologic degeneration and supporting evidence from x-rays, brain waves, lumbar puncture and other investigative procedures. Treatment is neurosurgical.

2. *Localized Headache Due to Superficial Trauma.* Occasion-

ally, patients complain of persistent headache well localized to the region in which the blow was inflicted. Such pain may be shown to be due to a traumatic neuritis of superficial nerves and secondary vascular dilatation by local infiltration with novocain® and may be relieved by local surgical excision of the affected nerve and artery.

3. *Injury to Cervical Structures Incurred at the Time of Head Injury.* Most head injuries of consequence occur as a result of forces which are likely also to cause cervical injury involving ligaments, disks or bones. They may be forgotten unless special examination for their presence is made. In such cases, physiotherapy, heat, traction and a Thomas collar may be of great benefit.

4. *Tension-Vascular Headache.* This is perhaps the most common and troublesome syndrome following head injury and seems to depend more on the emotional equilibrium of the injured victim than on the mechanical nature of the injury itself. Posttraumatic headache of this type is likely to be associated with feelings of vertigo, light-headedness, inability to concentrate, emotional lability and a lack of confidence. Circumstances of the accident, legal complications and compensation problems conspire with the "ripeness" of the individual for an emotional debacle to produce a syndrome which is difficult to relieve. Some patients in this category who had suffered from headaches of a migrainous sort before the accident develop an accentuated form of their migraine. In others, the factors which cause "tension" headache come into play. Prevention of this syndrome may be the most important aspect of therapy. This is best achieved by putting the patient back into circulation just as soon as it can be determined that no serious intracranial damage has occurred. Prolonged periods of bed rest and oversolicitousness on the part of the physician will promote the development of this state, whereas the fact that the doctor is confident that normal activity may be resumed at an early date may prove more beneficial than a thousand explanations and reassurances. The use of "tranquilizing" agents of the rauwolfia or meprobromate groups may be useful. In other patients, a trial of small doses of benzedrine® in combination with salicylate analgesics is more successful in relieving symptoms while rehabilitation is in progress.

HEADACHE DUE TO LOW CEREBROSPINAL FLUID VOLUME

Lumbar Puncture Headache

The most common example of this type is the headache which occasionally follows lumbar puncture. An essential criterion for its diagnosis is the fact that headache is present only when the patient is in the vertical position and disappears when he is horizontal. Headache following lumbar puncture which does not answer this description is due, at least in part, to other factors. Of these, anxiety and tension are the most common. Wolff (14) has shown that the headache which is due to lumbar puncture is based primarily on diminished volume of cerebrospinal fluid. Decreased CSF volume causes compensatory dilatation of the sensitive vascular structures which serve as the moorings of the brain and renders them more sensitive to the altered intracranial dynamics when the patient assumes the erect position. The amount of fluid usually withdrawn in a spinal tap (5–10 cc.) is not enough in itself to produce headache, but the subsequent leakage of spinal fluid through the needle hole in the dura creates a situation productive of headache when approximately 25–30 cc. has escaped. The decrease in CSF pressure in itself is not the cause of headache, but rather the decreased CSF volume.

In the case of headache following spinal anesthesia which is not affected by changes in the position of the patient, a sterile meningitis and radiculitis accompanied by pleocytosis in the spinal fluid is often the cause of the headache. Apparently this is the result of a drug allergy or idiosyncrasy, and may be helped by antihistamine or cortisone therapy. The treatment of the ordinary lumbar puncture headache, on the other hand, depends on the restitution of CSF volume. This is achieved by giving the patient adequate fluids and requiring that he stay flat until the needle hole in the dura has healed and temporary trial of the erect posture has demonstrated that it can be endured without the development of headache. Prevention of this syndrome may be aided by using as small a spinal needle as is compatible with the purpose of the tap, and by keeping the patient prone with the buttocks elevated for an hour after the puncture, followed by a period of 6 to 8 hours lying in the horizontal position.

Pneumoencephalography Headache

When spinal fluid is not only withdrawn but is replaced with air as in pneumoencephalography and ventriculography, vascular moorings are dilated and rendered extra-sensitive to the tug of a brain which suddenly becomes much heavier once it ceases to float in spinal fluid. Inhalation of pure oxygen in an effort to "wash out" nitrogen in the subarachnoid spaces is felt by some to hasten restitution to normal. Time, analgesics and sedation are the most practical measures.

Dehydration Headache

Headache due to low spinal fluid volume may be observed in clinical states involving severe dehydration and is relieved when fluid balance is restored.

FEVER, FOREIGN PROTEIN REACTION, "TOXIC" STATES

When 0.1 mg. of histamine is injected intravenously into a normal human being, a widespread dilatation of the vascular system takes place, associated with a sudden drop in blood pressure. The blood vessels in the dependent portions of the body apparently regain their original caliber before the cranial vasculature contracts, with the result that the latter receives the full force of the returning systemic pressure in a dilated state. The excessive dilatation and pulsation of the intracranial vessels which results causes severe throbbing headaches. This headache is not relieved by compression of the extracranial vessels by a blood pressure cuff or by infiltrating them with novocain®. The implication, therefore, is that the *intracranial* vascular dilatation is responsible for the major portion of such headache. This conclusion is supported by the fact that dampening the intracranial pulsations by raising CSF pressure to 800–1,000 cm. of water causes temporary cessation of the headache. When the intracranial dilatation comes to a natural close or the histamine effect wears off, headache ceases.

The headache which accompanies viral and bacterial infection,

septicemia or the injection of foreign protein, such as typhoid vaccine, has been shown (15, 16) to have a mechanism similar to that caused by the intravenous administration of histamine. Similar headaches are produced by periods of anoxemia in the brain following sudden drops in blood pressure, exposure to low oxygen concentration, as at high altitudes, or in carbon monoxide poisoning, or the post-ictal state. Ingestion or inhalation of nitrites causes similar painful intracranial vascular dilatation. Vasoconstrictive agents have minimal effect in reversing the process. Consequently, relief of this type of headache depends chiefly on analgesic agents, such as the salicylates and codeine.

THE TRUE NEURALGIAS

The true neuralgias are characterized by attacks of lancinating, lightning-like jabs of pain, closely limited to the area of sensory distribution of a cranial or cervical nerve. The type of pain, its localized distribution and its tendency to be set off by trigger mechanisms in the affected area are prerequisites to the diagnosis of a tic. Head pains which lack these characteristics should not be classified as "tics" or true neuralgias since the surgical therapy which is effective for "tic" may not only be ineffective for seemingly similar "aches," but actually may make matters worse. There is some evidence to suggest that such "tics" may result from ganglionic ischemia and in some patients vasodilators, such as nicotinic acid in generous dosage, may prove beneficial. Early enthusiasm for treatment with large amounts of thiamine chloride or liver extract has waned. Inhalation of trichloroethylene may offer temporary relief in trifacial neuralgia, but should be used with care in elderly patients subject to cardiac arrhythmias. Injections of the nerve or ganglion involved with alcohol or boiling water by a neurosurgeon may bring prolonged relief or may have to be followed by surgical ganglionectomy. It should be remembered that tumors of the ganglion, aneurysms in the vicinity of the ganglion and multiple sclerosis involving the ganglion may be a source of "tic." The exact mechanism of this disorder is not known, but a high degree of relief may be found in the hands of a competent neurosurgeon. Unfortunately, this is not true of the pain of herpes zoster.

MIGRAINE

Description and Diagnosis

The "classic" migraine attack is ushered in by the sudden onset of dramatic neurologic phenomena. In most cases it is the sensory rather than motor system which is affected, although rare examples of "neuroplegic" migraine have been recorded (17). The most common aura is visual, consisting of the development of an enlarging blind spot, usually in homonymous visual fields, but occasionally unilaterally. Scintillating and occasionally colored zig-zag lights often form its leading edge. Vision slowly returns in the wake of the spreading "prairie fire." Numbness of face, tongue and hand, or even complete hemianesthesia, aphasia, alexia, inability to concentrate, vertigo and, in rare cases, hemiparesis and ophthalmoplegia may be present in the initial stage only to give way to the development of headache, nausea and vomiting and general prostration. "The march" of the aura is slow, as compared with the rapid build-up of the epileptic aura. Not infrequently the aura is followed by no headache. On other occasions, it persists for a considerable period after the headache has set in. Should the neurologic symptoms of the aura outlast the headache or appear, not as an aura, but as a sequel to headache, suspicion should be aroused as to the possibility of organic intracranial disease.

When attacks of this type occur repeatedly in an otherwise healthy individual, especially when a family history of a similar disorder is obtainable, there is no difference of opinion as to the diagnosis of migraine. For every one of these "classic" attacks, however, approximately 10 attacks of "ordinary" sick headache are to be found in migrainous individuals. These are unaccompanied by neurologic aura, but are likely to last longer and have more unpleasant side effects, such as nausea, vomiting, diarrhea, polyuria, weakness and prostration. In some patients episodes of car-sickness, cyclic vomiting, vertigo, paroxysmal tachycardia (18), precordial pain (19) and abdominal pain may play the role of "migraine equivalents" and temporarily replace the patient's usual type of migraine for a period of weeks or months, only to have the original pattern of attacks recur. Some patients will exhibit at various periods in their life all the variations of

migraine, whereas others will always have the same type of attack. Similarly, some migrainous families will demonstrate among their members all the different types of migraine and others will present only one form of the disease. A familial tendency is present in about 80% of cases, and is therefore important in diagnosis.

The pain in migraine is usually, but not necessarily, unilateral. In the classic form of the disease, it occurs most often on the side of the head opposite the side of the neurologic symptoms. Occasional well-documented examples occur, however, of unilateral headache developing on the same side as the visual scotoma. The headache is described as pain, often of a throbbing type, made worse by bending over, coughing, straining and motion of the head. It is related in its distribution to the anatomy of the cranial blood vessels, especially the branches of the external carotid, rather than to any cranial nerve. It frequently involves the suboccipital area, the neck and trapezius area, and even, at times, the arm. In some patients, the pain affects alternate sides from one attack to another, but in some patients it always recurs in the same location. It tends to drive the patient to the seclusion of a dark, noiseless room. A residual hyperesthesia of the scalp is a frequent sequel to the pain. The pain may last only a few minutes, or it may persist for several days in severe attacks, and be accompanied by marked prostration requiring hospitalization. Occasionally the frequency of individual attacks may become so great that the patient is suffering continuous headache and may be said to be in "migraine status." During the attack, the presence of visibly dilated temporal vessels on the affected side may be of diagnostic significance and manual compression of such vessels, with resultant temporary relief of pain, is consistent with the mechanism and diagnosis of migraine. The successful relief of an attack of headache by the use of a vasoconstrictive drug, such as ergotamine tartrate, may be of diagnostic as well as therapeutic importance.

The tendency for migraine attacks to be precipitated by fatigue, emotional upsets, changes of pace in living and menstruation, and to occur in the early hours of the morning or on awaking, and on Saturdays, Sundays and holidays, is of some diagnostic help. The fact that they tend to disappear temporarily

during pregnancy (20), after operations and during serious illnesses, also helps to differentiate migraine from other types of headache which are not affected by these factors.

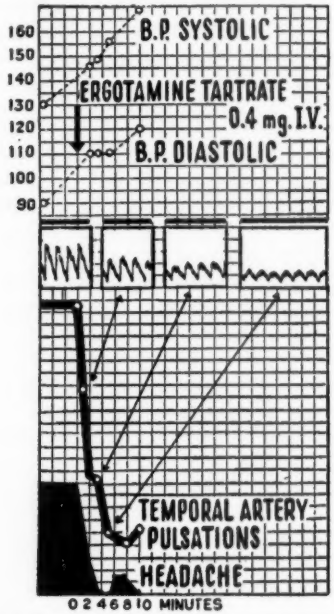

FIG. 2.—The ability of ergotamine tartrate to constrict the temporal artery, dampen its pulsations, and reduce headache is shown. In this acute experiment the intravenous route for the medication was used. When the ergotamine is given subcutaneously, its effect on cranial artery pulsation is more gradual and the decline in headache intensity is correspondingly slower.

The personal attributes of those who have migraine may help in the diagnosis. "Those who suffer severely . . . tend to be of a slender build, with quick, alert, intelligent responses to questions and situations. The personality is described as characterized by a keen sense of responsibility, a desire to please, overconscientiousness, a striving for perfection in all they do and a preference for

suppression of hostility rather than precipitation of 'scenes.' Such characteristics are by no means limited to migraine patients, nor do all migraine patients have them. Nevertheless, they are common enough to be considered corroborative evidence for the diagnosis when they are present" (21).

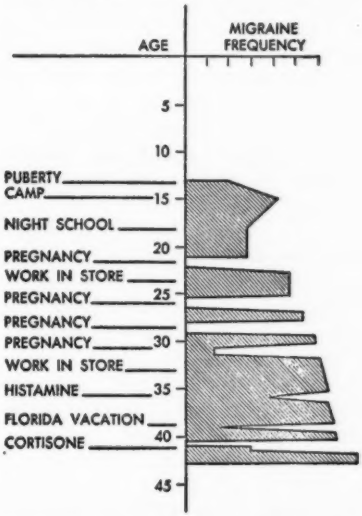

FIG. 3.—The beneficial effect of pregnancy on migraine is demonstrated. Vacation and cortisone similarly brought relief. The relentless progress of the disease under the stress of a crowded life, however, was only temporarily interrupted by these agents.

MECHANISM

Knowledge of the fundamental etiology of migraine is far from complete, but some of the immediate mechanisms are now understood. The best evidence (22) suggests that in the initial or neurologic phase of the migraine attack, vasoconstriction is taking place with resultant tissue ischemia. This can be relieved, if caught quickly enough, by small doses of cerebral vasodilators, such as nitroglycerin or CO_2. In the painful phase of the attack,

on the other hand, cranial blood vessels are dilated to a point where pain develops. This is relieved by a vasoconstrictor, such as ergotamine tartrate (23). In addition to the physical effect of the dilatation in stretching the sensitive vessel walls, factors as yet unknown are probably at work which render the wall of the vessel particularly sensitive to pain as a result of this dilatation (24).

A working concept of the dynamics of migraine may be derived from the following observations which seem to stand the test of time:

1. There is a strong factor of inheritance.
2. The cranial vasculature is intimately involved.
3. Migraine occurs in response to changes either within the body or in its environment requiring adaptation by the body. Exposure to stress of various sorts, of internal or external origin, brings more migraine; removal from stress or protection against it (for instance, pregnancy?) relieves migraine.
4. Patients with migraine who suffer from it most seem to be endowed with a personality that seeks and creates stress and a physiology that handles it poorly.

This leads to the concept that "the migraine patient has inherited a neurophysiologic system (affecting especially the behavior of cranial vessels, but also more widespread in its action) that is peculiarly susceptible to the deleterious effects of a variety of stresses; in many cases the patient is also endowed with a personality that in itself promotes the occurrence of stress. Since the inheritance of the migrainous tendency is a *fait accompli*, therapeutic efforts must be directed toward correction of the abnormal behavior of the cranial vessels during the acute attack, fortifying the sensitive vascular mechanism against future onslaughts, bolstering the total bodily economy so that it can better withstand strain, and teaching the patient new attitudes that will make it unnecessary to create stresses and easier to withstand those that everyone must endure" (25).

Treatment of the Acute Attack

Attempts to abort attacks of "classical" migraine by the immediate use of nitroglycerin, CO_2, nicotinic acid or other vasodilat-

ing drugs at the onset of the aura, have only limited practical usefulness. Occasionally, patients may find a dose of one of these drugs which, if administered at once, seems to shorten and mitigate the whole "classic" migraine attack. Most patients learn, however, that it is more practical to aim therapy from the outset at the painful secondary stage of vasodilatation. In general, the pain of migraine will be most successfully relieved with the least medication if adequate amounts of an effective drug are given early in the attack. Since attacks vary in severity, patients naturally hesitate to use powerful and sometimes upsetting vasoconstrictors for a mild attack which might respond to a cup of hot coffee and a couple of aspirin tablets. If relief by simple measures is not obtained within an hour, however, it is usually wisest to turn at once to the use of a more effective agent rather than to procrastinate further since, as the hours of headache go by, edematous changes in the wall of the affected artery may render it less responsive to pharmacotherapy, and more rather than less drug (as well as discomfort) will have to be tolerated. When attacks wake the patient from sleep at night, they are usually destined to be of a severity which demands "the heavy artillery" immediately. One principle is to provide a setting for recovery which is conducive to the needs of the occasion. The migraine attack arises out of stress, hurry and confusion, and will subside most quickly if peace, quiet and rest can be provided in addition to any form of drug therapy. Sometimes, when drugs such as ergotamine tartrate are effective in stopping the pain of an attack, the doctor and the patient tend to forget that more fundamental repair to the human mechanism than this rather superficial relief from pain is going to be necessary if the patient is not quickly to become a victim again. The physician can help the patient find a drug which is effective, but must also insist that he get mental and physical rest, the lack of which has produced his attack.

Some attacks are well controlled by mild sedatives, salicylates, caffeine and, if necessary, codeine. Injectable narcotics should never be placed in the hands of the patient or a member of his family. This applies to wives of physicians especially. Most patients who seek a doctor's advice for headache have tried the ordinary measures and have found them wanting. For them, the

DOSES OF VARIOUS ERGOT DERIVATIVES

NAME OF COMMERCIAL PRODUCT	COMPOSITION	FORM	ROUTE	USUAL INITIAL DOSE	MAXIMUM INITIAL DOSE	MAXIMUM AMOUNT IN 1 DAY
Gynergen®	Ergotamine tartrate 1 mg.	Tablet	Oral	1–3 tablets	5 tablets	10 tablets
Cafergot®	Ergotamine tartrate 1 mg. Caffeine 100 mg.	Tablet	Oral	1–2 tablets	3 tablets	6 tablets
Cafergot PB®	Ergotamine tartrate 1 mg. Caffeine 100 mg. Bellafoline 0.125 mg. Pentobarbital 30 mg.	Tablet	Oral	1–2 tablets	3 tablets	6 tablets
Wigraine®	Ergotamine tartrate 1 mg. Caffeine 100 mg. Acetophenetidin 130 mg. Belladonna alkaloids 0.1 mg.	Tablet	Oral	1–2 tablets	3 tablets	6 tablets
Bellergal®	Ergotamine tartrate 0.3 mg. Bellafoline 0.1 mg. Phenobarbital 20 mg.	Tablet	Oral	1–3 tablets	4 tablets	6 tablets
Cafergot® suppositories	Ergotamine tartrate 2 mg. Caffeine 100 mg.	Rectal suppository	Rectal	½–1 suppository	1 suppository	2 suppositories
Cafergot PB® suppositories	Ergotamine tartrate 2 mg. Caffeine 100 mg. Bellafoline 0.25 mg. Pentobarbital sodium 60 mg.	Rectal suppository	Rectal	½–1 suppository	1 suppository	2 suppositories
Gynergen®	Ergotamine tartrate 0.5 mg. per cc.	Ampoules (0.5 and 1 cc.)	Subcutaneous and intramuscular	0.3 cc.–1 cc.	1 cc.	1.5 cc.
			Intravenous	0.3 cc.–0.5 cc.	0.5 cc.	1 cc.
Dihydroergotamine (D.H.E. 45)	Dihydroergotamine methanesulfonate 1 mg. per cc.	Ampoules	Subcutaneous and intramuscular	0.75–1 cc.	1.5 cc.	3 cc.
			Intravenous	0.5 cc.	0.75 cc.	1 cc.

ergot derivatives offer the most help. A table of those commercially available, with suggested doses, is presented. It is believed that these drugs act mostly through their ability to constrict dilated branches of the carotid arteries. Their toxic effects depend largely on their vasoconstrictive ability. Immediate symptoms of nausea, vomiting, lassitude and muscle cramps are not

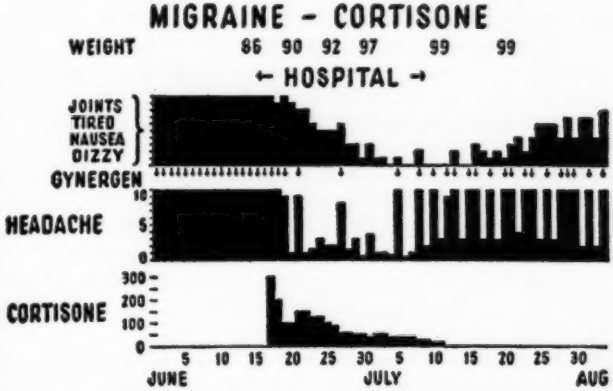

FIG. 4.—Cortisone's capacity to suppress migraine is demonstrated in this chart. It is also apparent that as cortisone is withdrawn, migraine recurs and soon reaches its precortisone severity.

uncommon. Chlorpromazine®, dramamine®, marezine®, atropine, caffeine and cortisone are helpful in offsetting these unpleasant side effects and often aid in the general recovery of the patient. Symptoms suggesting short-term or long-term ischemia of coronary or peripheral arteries should be regarded with respect.

Contraindications to the use of ergot are: (1) vascular disease, known or suspected, including disease of veins as well as arteries; (2) hypertension; (3) jaundice and liver disease; (4) severe sepsis, cachexia or anemia; (5) thyrotoxicosis; (6) pregnancy (dihydroergotamine, D.H.E. 45, may be used in the first two trimesters).

Further guiding principles in the use of ergot derivatives include:

"1. The ergot drug to fit the needs of the patient should be carefully selected, the dosage adjusted to the minimal effective amount and the side effects combated by suitable adjuvant drugs.

2. The patient should be instructed to use ergot as early in the attack as he can make the diagnosis of "one of his migraines." (Once the amount of ergot that is required for his attacks has been determined, he should be urged to use that amount at the start rather than to distribute it over several hours.)

3. He should be warned of possible side effects, and at the same time told that they usually can be successfully combated if they occur. (An unexpected bad reaction destroys the patient's confidence in both medicine and doctor.)

4. Ergot derivatives should not be considered a failure until ergotamine tartrate has been given early in an attack, by the parenteral route.

5. The patient's schedule should be lightened on the day of a headache, even if relief has been produced by ergotamine.

6. Regarding the amount and frequency of dosage of ergot derivatives, the data presented in the table on page 34 are offered for use as a guide.

7. Intravenous administration should be avoided except in rare emergencies, and when the patient's tolerance is well understood.

8. There should be at least 2 days in each week when no ergot is used.

9. If symptoms of toxicity of a more than transitory nature begin to appear, ergot should be stopped at once" (26).

Dihydroergotamine is not as powerful an agent against headache as ergotamine tartrate, but some patients can tolerate it who cannot take ergotamine tartrate.

The most reliable and efficient route of administration is the parenteral one (IM or SC). For most patients, however, the rectal route provides the best combination of convenience and effectiveness. An oral agent, such as chlorpromazine®, dramamine® or, in some cases, cortisone, taken at the onset of an attack, combined with the simultaneous rectal use of a caffeine-ergotamine suppository, is an effective combination for many patients.

"Methyl-iso-octenylamine (octin®-hydrochloride) acts in some patients as a vasoconstrictor, and for them may prove useful in stopping headache. Because of its tendency to cause transitory hypertension, a trial dose of 50 mg. should first be administered intramuscularly, and the blood pressure checked. Provided no alarming hypertension results, this drug may be used in a dose of 50-200 mg. intramuscularly. Oral and rectal administration of octin®, for the acute attack, is rarely effective. Octin® should not be given to hypertensives, but may be used during pregnancy. MacNeal reports that a combination of 50 mg. of octin® and 1 cc. of D.H.E. 45 is effective" (27, 28).

Patients occasionally receive relief from an acute attack by the use of thiamine chloride (29), dramamine® injectable (30), sodium nicotinate (31), ACTH, cortisone, inhalation of 100% oxygen, triethylene, 10% CO_2 and injections of procaine in the region of the affected artery (32).

Prevention of Attacks

No single, specific regimen of treatment has been discovered that will prevent migraine. Vitamins, diets, hormones, psychoanalysis, vasoconstrictors, vasodilators, sedatives, stimulants, bile salts, surgery, hydrotherapy, physical therapy—all have proved helpful in certain patients when administered by certain doctors. There has been no "insulin" found for migraine which will affect the disease in a predictable fashion from patient to patient and doctor to doctor. This fact is no reason for telling the patient that there is nothing that can be done for migraine. Many drugs may be helpful in reducing the frequency and severity of attacks and much can be done by a sympathetic physician in "the gradual education of the patient so that he will adjust his work and his methods of living to the personality and the nervous system which he has inherited" (33). An interested family physician can achieve this goal, in most cases, as well as, or better than, the expert psychiatrist, and it is relatively rare that the latter needs to be called in, provided that the family physician is willing to take the time necessary with his patient to work out changes in ways of living. When the patient finds in his doctor belief in his symptoms, patience to hear him out, willingness to work at

his problem over a period of time, and hope that some measure of relief may be achieved, he will be more willing to fulfill his own share of the therapy in making the alterations that are required of him.

Some common errors in living which lead to migraine are: (1) Poor and irregular meals; (2) hectic deadlines; (3) sleeping late on Saturdays, Sundays and holidays; (4) lack of breaks in the day; (5) overcrowded schedules; (6) excessive participation in community and church projects; (7) overanxiety regarding preparations for guests, shopping and other trips; (8) lack of exercise; (9) lack of recreation, avocation and vacation; (10) aiming for impossible goals; (11) suffering petty wrongs in silence; (12) failure to get away periodically to enjoy "time for oneself."

The physician can gradually help his patient to understand and alter these and many other individual sources of fatigue and to *believe* in the necessity for eliminating them if migraine is going to be alleviated.

References are herewith given to the use of various regimens and agents in use for the prevention of migraine: histamine (34), hormones (35–39), antihistamines (40), vitamins (41), diets (42, 43), bile salts (44), potassium thiocyanate (45), calcium and potassium salts (46), head traction (10) and procaine infiltration (9). All these agents have had some success in some hands at some period. None has been specific. Recently, drugs of the "tranquilizing group" have proved to be occasionally effective in reducing the frequency of migraine attacks, but none has served to eliminate them. In isolated instances, neurosurgeons have met with success in eliminating migraine which is confined to a well-localized area by interruption of sensory or sympathetic nerve pathways, or by ligation of involved arteries. Consultation with an experienced neurosurgeon is advised before such a surgical approach.

The short term use of ergot derivatives in a prophylactic way seems justified in some patients to protect them against attacks at certain limited periods when experience has shown that headache is likely to be particularly inconvenient or prevalent. Such occasions include weddings, funerals, graduations, the menstrual period, weekends, the beginning and ending of vacation and other periods involving major changes of pace.

Migraine Status

Fortunately, this state is attained by only a few patients. It consists of a running together of individual attacks until life is one constant headache. The patient often is suffering also from nausea, lassitude, weakness, malnutrition, joint pains, depression and the effects of an accumulation of drugs, including too much ergot, barbiturates and narcotics. Hospitalization for at least a month, followed by a prolonged period of rest at home or in a convalescent home is usually necessary if a significant dent is going to be put in this most depressing disease. Two weeks of a hospital regimen is frequently required before the headache begins to lift. During this period, the physician must establish a firm bond with the patient so that he may gain his co-operation in getting rid of his bottles of pills, multiple injections and despair. Patience, reassurance, understanding and firmness in big doses are required. Good food, peace and complete freedom from responsibility are important. A single room is essential. Occasionally, steroid therapy for a short period, or the use of insulin to stimulate appetite, is helpful. Chlorpromazine® has been useful during the period when more potent drugs are being withdrawn. Frequently such patients have been taking ergot daily. Its removal results in a bad headache for a few days (which must be controlled by non-vasoconstrictors), but leads to an eventual unwinding of the vicious circle. Re-education and suitable alterations of plans for the future should be undertaken before the patient is permitted normal activity, or the good work will be undone.

ATYPICAL FACIAL NEURALGIA

This syndrome of pain in the face or one side of the head usually follows a vascular rather than a sensory nerve distribution and may spread to the neck and arm. The pain is always present and simulates an aching tooth or sinus. It may be punctuated with periods of greater severity, usually of a throbbing nature. It does not have the electric shocklike quality of tic nor are "trigger" areas often present. Carotid compression often alleviates it temporarily, suggesting that a vascular component akin to migraine is a factor in its mechanism. Operations rarely relieve

it. Addiction is common. In such patients hysteria, or an underlying major psychosis, is not too uncommon. Keeping these unfortunate individuals from becoming addicts, preventing operations which add new symptoms to an already impressive set and maintaining the patient in a condition in which he or she can be employed are goals which should be considered acceptable in this condition.

"HISTAMINIC CEPHALGIA"

"Horton's syndrome," ("autonomic cephalgia") is a well-defined syndrome which clinically does not behave like migraine, but which seems to share with migraine localized vasodilatation of branches of the external carotid artery as the immediate mechanism of pain. Clinically it consists of batches or clusters of headache, mostly in men, occurring every day or night and often several times in a day or night for several weeks or months on end, followed by headache-free periods of months or years. In some patients only one or two "clusters" will occur in a lifetime. In others, "clusters" of active headache may grow in duration, and periods of freedom decrease, until, in rare cases, there is a constant daily recurrence of the attacks over periods of years. The attack is short in duration and severe enough to make men cry and pace the floor and even contemplate suicide.

Its onset is fairly abrupt. The first symptom is likely to be a full, burning feeling in the temple or eye and the development over 5 or 10 minutes of severe pain in the temple, forehead, eye, cheek and, not infrequently, the region behind the ear and upper part of the neck, accompanied often by tearing, miosis, enophthalmos and vascular engorgement of the affected eye, homolateral blocking of the nose and rhinorrhea, flushing and sweating of the face and, occasionally, by nausea and excess salivation. It frequently wakes the patient from sleep and causes him to pace the floor, and to press his temple with his hand or squeeze it against his upraised inner arm and carry on in a frantic manner for a span of a few minutes to 2 or 3 hours until relief is obtained by medication or until the attack subsides spontaneously as suddenly and mysteriously as it came. During the phase in which these attacks are prevalent, the administration of a vasodilator

(such as histamine acid phosphate, 0.35 mg. subcutaneously or alcohol or one of the nitrites) will frequently precipitate a characteristic attack about 10 to 30 minutes later. Powerful vasoconstrictors, such as adrenalin®, ergotamine, and ergotamine-caffeine mixtures will frequently bring the attack to a close within 10 to 15 minutes. These facts led Horton (47) to believe that histamine is the chemical in the body which is the cause for these attacks and that "desensitizing" the patient to histamine either by the subcutaneous or intravenous route would lead to relief. Since the "clusters" of headache spontaneously come to an end and since no control studies have been published, it is difficult to say whether histamine desensitization actually is an effective regimen. When these patients are brought into a hospital and put at "legalized" rest, their attacks tend to cease, no matter what regimen is used. Antihistaminic therapy is not usually effective. ACTH and cortisone may prove useful in bringing a cluster to a close, but since these patients have a propensity for duodenal ulcers, the use of steroids should be preceded by gastrointestinal x-rays and accompanied by the use of atropine derivatives, antacids and an ulcer diet. One or two wigraine® tablets (or a cafergot PB® suppository, or an injection of 0.5 to 1.00 cc. of gynergen®) is the most effective measure in stopping an individual attack.

It has been the author's observation that this type of headache tends to occur in very active, intense men (who rarely take vacations) during or following prolonged periods of strain. In order to get them out of a "cluster," it is important to get them rested. Relief from the devastating effect of the headache is a cardinal point in the program. In patients who exhibit no contraindications to the use of ergot, a program of prophylactic use of ergot twice or three times a day is mapped out. This is usually in the form of one half a cafergot PB® suppository, or 0.5 cc. of gynergen® subcutaneously, on arising and at bedtime; or two bellergal® tablets before meals and at bedtime. Such a regimen often prevents headaches from developing and allows the patient to relax and get rested. Should a headache break through this regimen, either 0.5 cc. of gynergen® or one half a cafergot PB® suppository, or a wigraine® tablet is allowed once during the twenty-four hours. Beyond this, codeine and aspirin must suffice.

Meprobromate with meals and at bedtime helps. The patient is asked to discontinue alcohol, at least temporarily, and it is essential that his schedule be lightened or stopped. After a week of such a program, prophylactic doses of ergot are reduced and the effect noted. If no recurrence is met after further observation, further reduction is made until the "cluster" has come to an end. In my hands, this regimen has met with more success than histamine "desensitization" and no untoward effects of ergot have been encountered.

TENSION HEADACHE

Last, but far from least, comes the tension headache. Patients with this disorder frequently describe it in terms of a "fullness," "drawing," "tightness," or "binding," a "discomfort" all over the head. Pain is present in the more severe forms and is likely to involve particularly the occipital areas and the neck. Such headaches may be transitory or may persist for days, weeks or even months. They occur during and after periods of anxiety in tense persons. Their mechanism has been shown by Simons *et al.* (48) to consist in part of excessive spasm of neck and scalp muscles, and further evidence is currently developing to indicate that vascular constriction and ischemia of muscles and nerves may also play a role (49). In connection with this, Brazil (50) has shown that the intravenous use of sodium nicotinate brings relief. The vasoconstrictor drugs are of little benefit, as compared to their high degree of efficacy in migraine. By and large, analgesics of the caffeine, salicylate variety are the most useful in therapy, one of the best being fiorinal®, which contains also a short-acting barbiturate. For prevention, the tranquilizing agents of the meprobromate, reserpine and barbiturate group are often helpful. The more fundamental attack, however, must be directed toward relieving the patient's anxiety. In most instances the family doctor, again, can supply what is needed in this sphere if he is willing and can take the time to do it. In severely disabled patients in whom the symptoms are constant and incapacitating, more formal psychotherapy must be sought. This is particularly true of those patients in whom "headache" has become the presenting symptom of a depression or conversion hysteria.

Although drugs for the immediate relief of symptoms may be justified at the outset of therapy, they will rarely prove to be of permanent benefit. Through repeated, and often time-consuming, visits the patient must be led to understand the causal relation between his symptoms and his anxieties and steered into talking about his problems, rather than dwelling on the fascinating variations of his headache or the effects of his most recent medicine. Many of the measures which have been outlined under *migraine* apply also to the *tension* patient in regard to managing his daily life and attitudes. A pinch of medicine, a sprinkle of physiology, a good helping of patience and understanding and a major portion of common sense will help many of these patients to more healthy, happy lives.

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